Remarks/Arguments

Reconsideration of the above-identified application in view of the present amendment is respectfully requested.

By the present amendment, claims 1, 54, and 57 have been amended to recite that the $CD133^+/CD34^+$ hemangioblast cells and mesenchymal stem cells are isolated and purified from bone marrow mononuclear cells and once isolated and purified, enriched at least two-fold prior to administration to the subject. Support for this limitation can be found in Examples 3 and 4 of the specification. Claim 1, 54, and 57 have also been amended to delete the phrase "without leucopheresis or culturing the cells".

Below is a discussion of the 35 U.S.C. §112, first paragraph, rejection of claims 1-2, 4, 10-12, 21, 23-36, 40-43, 50-54, 56-57 and 62-69, and the 35 U.S.C. §103(a) rejection of claims 1-2, 4, 10-12, 21, 23-36, 40-43, 50-54, 56-57, and 62-69 that was originally made in the Office Action dated April 11, 2007 (hereinafter, "the April 11th Office Action").

1. **35 U.S.C. §112, first paragraph, rejection of claims 1-2, 4, 10-12, 21, 23-36, 40-43, 50-54, 56-57 and 62-69.**

Claims 1-2, 4, 10-12, 21, 23-36, 40-43, 50-54, 56-57, and 62-69 were rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement. The Office Action argues that the amendment to claims 1, 54, and 57 introducing the phrase "without leucopheresis or culturing cells" lacks any basis in the instant application.

By the present amendment, the phrase "without leucopheresis or culturing cells" has been removed from claims 1, 54, and 57.

Accordingly, Applicants respectively submit that the 35 U.S.C. §112, first paragraph, rejection of claims 1, 54, and 57 is rendered moot, and request that the 35 U.S.C. §112, first paragraph, rejection of these claims be withdrawn. Additionally, Applicants respectively request that the 35 U.S.C. §112, first paragraph, rejection of claims 2, 4, 10-12, 21, 23-36, 40-43, 50-53, 56 and 62-69, which depend either directly or indirectly from claims 1, 54, and 57, be withdrawn.

2. 35 U.S.C. §103(a) rejection of claims 1-2, 4, 10-12, 21, 23-36, 40-43, 50-54, 56-57 and 62-69.

The Office Action states that removal of the phrase "without leucopheresis or culturing cells" may result in the reinstatement of the 35 U.S.C. §103(a) rejection of claims 1-2, 4, 10-12, 21, 23-36, 40-43, 50-54, 56-57, and 62-69 that was originally made in the April 11th Office Action.

In the April 11th Office Action, claims 1-2, 4, 10-12, 21, 23-36, 40-43, 50-54, 56-57, and 62-69 were rejected under 35 U.S.C. §103(a) as being unpatentable over Strauer *et al.*, *Circulation* 106:1913-1918, 2002 (hereinafter, "Strauer") taken in view of Shake *et al.*, *Annals of Thoracic Surgery* 73:1919-1926, 2002 (hereinafter, "Shake"), U.S. Patent Pub. No. 2002/0037278 A1 to Ueno *et al.* (hereinafter, "Ueno"), Kocher *et al.*, *Nature Medicine* 7:430-436, 2001 (hereinafter, "Kocher"), and U.S. Patent Pub. No. 2003/0199464 A1 to Itescu.

The April 11th Office Action argues that: Strauer teaches enriching CD34+/CD133+ endothelial progenitor cells from BM-MNCs; Kocher teaches methods for enriching such cells to 98%; and Shake teaches isolating and enriching

bone marrow-derived mesenchymal stem cells. From this, the Office Action argues that one having ordinary skill in the art would have been motivated to enrich the CD34+/CD133+ endothelial progenitor cells of Strauer using the method of Kocher because Kocher recognized that CD133+ cells promote vascularization. Additionally, the Office Action argues that one having ordinary skill in the art would have been motivated to combine Strauer and Kocher with Shake because all the references are directed to a common purpose, *i.e.*, promoting healing after myocardial infarction.

Should removal of the phrase "without leucopheresis or culturing cells" result in reinstatement of the previously made 35 U.S.C. §103(a) rejection, Applicants respectively submit that claims 1, 54, and 57 are patentable over Strauer in view of Kocher, Shake, Ueno, and Itescu because the combination of these references does not disclose teach or suggest to the skilled artisan isolating CD34+/CD133+ endothelial progenitor cells from bone marrow mononuclear cells 1 and enriching the isolated CD34+/CD133+.

Strauer does not teach or disclose isolating and enriching CD34+/CD133+ endothelial progenitor cells from bone marrow mononuclear cells. Strauer discloses that mononuclear cells harvested after overnight culture consisted of 0.65±0.4% AC133-positive cells and 2.1±0.28% CD34-positive cells (p. 1914, col. 2). Strauer does not disclose, however, that the harvested mononuclear cells were AC133- and CD34-positive endothelial progenitor cells. Rather, Strauer merely discloses that the harvested cells contained two different cell populations, *i.e.*, those that are CD34+ and those that are CD133+. Additionally, Strauer does not disclose that the

harvested cells are endothelial progenitor cells. In fact, Strauer acknowledges that adult, mononuclear bone marrow cells contain a variety of different cell stem and progenitor cell populations, such as mesodermal progenitor cells, hematopoietic progenitor cells, and endothelial progenitor cells (p. 1916, col. 2) and, thus, "several different fractions of mononuclear bone marrow cells may contribute to the regeneration of necrotic myocardium and vessels" (p. 1917, col. 1). In other words, it is unclear from Strauer as to which of the above-cited cell populations was actually contributing to the regeneration of necrotic myocardium and vessel formation.

Kocher does not teach or disclose a method for isolating and enriching CD133+/CD34+ endothelial progenitor cells. Kocher teaches that cytokine-mobilized mononuclear cells were separated into two fractions using a monoclonal antibody against CD34 (> 98% purity) (p. 430, col. 2). Kocher also discloses that within the CD34+ cell fraction, a subset displayed phenotypic characteristics of endothelial progenitors, including co-expression of Tie-2+ and AC133+ (p. 431, col. 2). Kocher does not disclose, however, that the subset of CD34+/AC133+ cells were enriched to 98% purity. The instant application teaches that expression of CD34 is temporal and can be influenced. For example, Figures 3 and 8 of the instant application show that CD133+ cells may or may not express CD34, and that such expression is effected by culture conditions. This demonstrates that in a given fraction of bone marrow-derived mononuclear cells, there are CD133+, CD34+, and AC133+/CD34+ cells. Thus, simply because the CD34+ cells were enriched to 98% purity does not necessarily mean that the subset of CD34+/AC133+ cells were also enriched to 98% purity.

Accordingly, Applicants respectively submit that claims 1, 54, and 57 are patentable over Strauer in view of Kocher, Shake, Ueno, and Itescu, and request that the 35 U.S.C. §103(a) rejection of these claims be withdrawn. Additionally, Applicants respectively request that the 35 U.S.C. §103(a) rejection of claims 2, 4, 10-12, 21, 23-36, 40-43, 50-53, 56 and 62-69, which depend either directly or indirectly from claims 1, 54, and 57, be withdrawn.

In view of the foregoing, it is respectfully submitted that the present application is in condition for allowance, and allowance of the present application is respectfully requested.

Please charge any deficiency or credit any overpayment in the fees for this matter to our Deposit Account No. 20-0090.

Respectfully submitted,

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